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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,565	10/17/2001	Thomas J. Gardella	0609.4730000	4604

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EXAMINER

HOWARD, ZACHARY C

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 08/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/869,565

Applicant(s)

GARDELLA ET AL.

Examiner

Zachary C. Howard

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20 and 22-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20 and 22-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 5/9/03; 11/6/03; 6/8/05
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Sequence Alignment #1 & #2

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DETAILED ACTION

The Art Unit location and the examiner of your application in the PTO have changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Zachary C. Howard, Art Unit 1646, Technology 1600.

Status of Application, Amendments and/or Claims

The amendment of 5/13/05 has been entered in full. Claims 20 and 24-28 have been amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 20 and 22-28 are under consideration in the instant application.

Information Disclosure Statement

The information disclosure statement filed 5/9/2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

Specifically, there is no copy of either of the following references:

- 1) Reference AS, Barbier et al. 1997.
- 2) Reference AT, Chorev et al. 1990.

Due to the absence of the copy of each reference, each citation on the IDS of 5/9/2003 has been crossed out, and Applicant is requested to submit this reference with a new Information Disclosure Statement. The examiner notes that a copy of each of the other references cited on the IDS of 5/9/03, 11/6/03, and 6/8/05 is present and each reference has been fully considered.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (12/13/04).

The rejection of claims 20 and 22-28 under 35 U.S.C. § 112, first paragraph at pg 3 for failing to provide enablement for the deposited cDNA clone is *withdrawn* in view of Applicants' affidavit which provides assurance that the deposit will be maintained and replaced if it should ever become unviable.

The rejection of claims 20, 22, 23 and 28 under 35 U.S.C. § 112, first paragraph at pg 3-4 for failing to provide enablement for agonists or antagonists that are 95% identical to SEQ ID NO: 2 is *withdrawn* in view of Applicants' amendments to the claims. Please note that the rejection of claims 24 and 27 is not withdrawn; please see claim rejections below.

The rejection of claims 20, 22, and 23 under 35 U.S.C. § 112, first paragraph at pg 4 for lacking written description is *withdrawn* in view of Applicants' amendments to the claims. Please note that the rejection of claim 24 is not withdrawn; please see claim rejections below.

The rejection of claims 20 and 22-28 under 35 U.S.C § 112, second paragraph, at pg 4-5 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is *withdrawn* in view of Applicants' amendments to the claims to read "from about residue 26 to about residue 181".

The rejection of claims 20, 22-24, and 27-28 under 35 U.S.C § 112, second paragraph, at pg 5 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is *withdrawn*. The previous Office Action asserted "If applicants mean a deletion spanning residue 26 to residue 181, it is impossible for a polypeptide to have this deletion and be 95% identical to SEQ ID NO: 2." It is noted that SEQ ID NO: 2 is the sequence of the wild type receptor with a deletion from about residue 26 to about residue 181. Therefore, because SEQ ID NO: 2 itself has this deletion, it is possible for another polypeptide to have both the indicated deletion and be 95% identical to SEQ ID NO: 2. For this reason, the rejection is withdrawn.

Please see new claim rejections below.

Claim Rejections - 35 USC § 112, 1st paragraph, scope of enablement

Claims 24 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method using cells comprising a polynucleotide encoding a polypeptide at least 95% identical to SEQ ID NO: 2, does not reasonably provide enablement for a polynucleotide at least 95% identical to a polynucleotide encoding SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 24 and 27 encompass methods with cells comprising a polynucleotide at least 95% identical to a polynucleotide encoding SEQ ID NO: 2. Instant SEQ ID NO: 1 is a polynucleotide encoding a polypeptide of SEQ ID NO: 2. The open coding region of SEQ ID NO: 1 is 1305 nucleotides. The genus of polynucleotides that are at least 95% identical to a sequence of 1305 nucleotides encompasses those with 1240 or more identical nucleotides. In other words, up to 65 nucleotides can be changed in the coding sequence of SEQ ID NO: 1 and still have a polynucleotide at least 95% similar to SEQ ID NO: 1. The genus includes those polynucleotides in which each of the 65 nucleotide changes are each in a different codon. Therefore, the genus encompasses those polynucleotides that encode polypeptides with up to 65 different amino acids from SEQ ID NO: 2, a polypeptide of 435 amino acids. Therefore, the genus of encompass polynucleotides encompasses those polypeptides with up to 65 changes in a polypeptide of 435 amino acids. In other words, this genus encompasses polynucleotides encoding polypeptides with 370 out of 435 amino acids of SEQ ID NO: 2, or up to 85% similarity.

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While the specification teaches the functionality of a receptor of SEQ ID NO: 2, the breadth of the claims is such that the claims encompass method using variants in which one or more amino acids of SEQ ID NO: 2 are substituted, deleted, and/or inserted. Claims 24 and 27 encompass a polynucleotide encoding a polypeptide, that comprises an amino acid sequence that is at least 85% similar to SEQ ID NO: 2 (as explained above), and can increase intracellular cAMP levels when activated by PTH or PTH-related peptide.

Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible variants of polypeptides of SEQ ID NO: 2. The specification has not provided a working example of the use of a variant of the polypeptide of SEQ ID NO: 2, nor sufficient guidance so as to enable one of skill in the art to make such a variant. The specification has failed to teach which amino acids of SEQ ID NO: 2 could be modified so as to produce a polypeptide that is not identical to SEQ ID NO: 2 and yet still retain a characteristic of the parent polypeptide, e.g., the functionality of increasing intracellular cAMP levels when activated by PTH or PTH-related peptide.

Applicants have not given any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property, or defined a difference in structure, or difference in function, between the protein corresponding to SEQ ID NO: 2 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 2 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 2, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 2. Conversely, if a protein variant of SEQ ID NO: 2 need not have a disclosed property, then the specification has failed to teach how to use such a variant.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence

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where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al.* (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, it may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39; Doerks *et al.* (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature

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Biotechnology 15:1222-1223; Brenner (April 1999) "Errors in genome annotation."
Trends in Genetics 15(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in
sequence databases but watch out for the traps." Trends in Genetics 12(10): 425-427].

Due to the large quantity of experimentation necessary to generate the large number of variants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

It is noted that a rejection under 112, 1st paragraph, scope of enablement was first made for claim 24 in the Office Action of 5/18/04 (see pg 7-8). In the final rejection of 12/13/04, this rejection was maintained for claim 24 and applied to new claim 27 (see pg 3). It is further noted that the original rejection only considered that the claims encompassed polynucleotides encoding polypeptides at least 95% identical to SEQ ID NO: 2. As explained in the rejection above, in actuality claims 24 and 27 encompass at genus of polynucleotides polypeptides at least 85% identical to SEQ ID NO: 2. For this reason, a new rejection has been made above in order to clearly set forth the basis of the rejection. The new rejection above supercedes the previous rejection of 5/18/04. However, Applicant's arguments (5/13/05) as they pertain to the previous rejection have been fully considered as they apply to the new rejection.

Applicant's arguments (5/13/05) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response dated 5/13/05 Applicant submits that the claims have been amended to recite that the polypeptide "increases intracellular cAMP levels when activated by PTH or PTH-related peptide" and requests that the rejection be removed.

Applicant's arguments have been fully considered but are not found persuasive.

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The examiner acknowledges that the functional limitation does restrict the encompassed genus to those polypeptides that would work in the assay. However, the claim language still allows for an extremely large number of sequence variants. As explained above, the claim language reciting "a polynucleotide having a nucleotide sequence at least 95% identical to a sequence...encoding... SEQ ID NO: 2" actually represents a genus of polypeptides at least 85% identical to SEQ ID NO: 2. Due to the extremely large number of variants in this genus, combined with the lack of teachings as to what changes that can be made to SEQ ID NO: 2 that still result in a functional receptor, one of ordinary skill in the art would need to engage in undue experimentation (as described in the above rejection) to practice the claimed method.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 24 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. § 112, paragraph 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicants are claiming and what Applicants have possession of.

Claims 24 and 27 are genus claims because the claims are directed to methods of using cells comprising polynucleotides encoding polypeptides with 85% or greater similarity to SEQ ID NO: 2, wherein the polypeptide increases intracellular cAMP levels when activated by PTH or PTH-related peptide. The genus of encoded polypeptides is highly variant because a significant number of structural differences between genus

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members are permitted. However, the instant specification fails to describe the entire genus of methods that are encompassed by each of these claims.

From the specification, it is clear that Applicants has possession of method of using a cell comprising a polynucleotide encoding SEQ ID NO: 2. The specification fails to describe or teach any other polypeptide which lacks the sequence of SEQ ID NO: 2 and increases intracellular cAMP levels when activated by PTH or PTH-related peptide. The claims, however, are not limited to a method of using a polynucleotide encoding SEQ ID NO: 2.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the genus of polypeptides encoded by the polynucleotides used in the claimed methods. There is not even identification of any particular portion of the structure that must be conserved. Structural features that could distinguish encoded polypeptides in the genus from others in the protein class are missing from the disclosure. The specification and claims do not provide any description of what changes should be made. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of

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distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only methods using cells comprising a nucleic acid encoding SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

It is noted that a rejection under 112, 1st paragraph, written description was first made for claim 24 in the Office Action of 5/18/04 (see pg 8-9). In the final rejection of 12/13/04, this rejection was maintained for claim 24 (see pg 3). It is further noted that

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the original rejection only considered that the claims encompassed polynucleotides encoding polypeptides at least 95% identical to SEQ ID NO: 2. As explained in the above, in actuality claims 24 and 27 encompass at genus of polynucleotides polypeptides at least 85% identical to SEQ ID NO: 2. For this reason, a new rejection has been made above in order to clearly set forth the basis of the rejection. The new rejection above supercedes the previous rejection of 5/18/04. However, Applicant's arguments (5/13/05) as they pertain to the previous rejection have been fully considered as they apply to the new rejection.

Applicant's arguments (5/13/05) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response dated 5/13/05 Applicant submits that the claims have been amended to recite that the polypeptide "increases intracellular cAMP levels when activated by PTH or PTH-related peptide" and requests that the rejection be removed.

Applicant's arguments have been fully considered but are not found persuasive.

The examiner acknowledges that the functional limitation does restrict the encompassed genus to those polypeptides that would work in the assay. However, the claim language still allows for an extremely large number of sequence variants. As explained above, the claim language reciting "a polynucleotide having a nucleotide sequence at least 95% identical to a sequence...encoding... SEQ ID NO: 2" actually represents a genus of polypeptides at least 85% identical to SEQ ID NO: 2. Due to the extremely large number of variants in this genus, combined with the lack of teachings as to what changes that can be made to SEQ ID NO: 2 that still result in a functional receptor, one of skill in the art could not identify which members of the large genus actually meet the functional limitation. Therefore, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20 and 22-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 and 22-26 are indefinite because it is unclear how measuring cellular cAMP accumulation leads to the identification required by the preamble of an agonist or antagonist of PTH receptor activity. It is unclear what outcome leads to the identification of a "agonist" or "antagonist". Can a decrease in activity identify a test compound that is both an agonist and antagonist? Clarity could be added to the claim by, for example, adding at the end a phrase such as, "wherein an agonist of the PTH receptor activity is identified by _____ (e.g., an increase in intracellular cAMP levels) in the presence of the test compound as compared to the absence of the test compound..." Note that there must be basis in the specification for the type of response and the suggestions made by the examiner do not necessarily have basis but are intended to present the general idea of concepts that may be suitable.

Claims 27 and 28 are similarly indefinite because it is unclear what outcome of "determining whether said iodinated test compound competitively binds to said rōNt polypeptide" leads to the identification of an agonist and what outcome leads to identification of an antagonist.

Claims 20 and 24-28 are also indefinite in that they recite acronyms such as "rōNt". Use of acronyms results in indefinite language because the acronyms used to define proteins can be subject to change or reference more than one protein. Therefore, when used for the first time scientific terms should be completely spelled out. Claims 22 and 23 are indefinite in this regard because they depend from claim 20 but the additional limitations do not render the claims definite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 22, 23 and 28 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by U.S. Patent No. 5,494,806 (cited previously by the Examiner on the PTO-892 of 2/12/2004).

It is noted that claims 20 and 22-23 were previously rejected under 102(b) as being anticipated by the '806 patent in the Office Action of 5/18/04 (see pg 9), and that this rejection was withdrawn in the previous Office Action of 12/13/04 (see pg 3). However, this rejection should not have been withdrawn 12/13/04 because the amended claims are still anticipated by the '806 for the following reasons.

Claim 20 is drawn to a method of screening for an agonist or antagonist of PTH receptor activity comprising contacting cells expressing a genus of rōNt polypeptide with a test compound. The genus of rōNt polypeptide encompassed by the claim includes any polypeptide that is at least 95% identical to the sequence from "about position 1 to about position 435 in SEQ ID NO: 2, wherein the extracellular amino-terminal ligand binding domain is deleted." The extracellular binding domain is further defined in the claim as having "an amino sequence from about residue 26 to about residue 181 in wild-type PTH receptor." However, as indicated in the specification, SEQ ID NO: 2 is the sequence of the wild-type PTH receptor with said domain deleted. Therefore, the phrase "wherein the extracellular amino-terminal ligand binding domain is deleted" does not in any way modify SEQ ID NO: 2, because this is an inherent characteristic of SEQ ID NO: 2. Furthermore, position 1 to position 435 represents the entire SEQ ID NO: 2 sequence. Therefore, the genus rōNt polypeptides encompassed by the claim includes any polypeptide that is at least 95% identical to SEQ ID NO: 2.

The '806 patent teaches SEQ ID NO: 3, which is a nucleic acid sequence encoding a rat PTH receptor amino acid sequence that is 96.1% identical to instant SEQ ID NO: 2 (an alignment of these sequences is attached to this Office Action as Sequence Alignment #1). The '806 patent further teaches that the PTH receptor stimulates cAMP accumulation when activated PTH (see col 9, lines 14-15). The '806

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patent further teaches screening assays to test compounds for agonistic or antagonistic properties using the cAMP accumulation (see col 22, lines 65-67). Therefore, the '806 patent clearly anticipates instant claims 20, 22 and 23.

Claim 28 encompasses a method with the same limitations as claim 20, except that the test compound is iodinated and the method comprises determining whether the iodinated test compound competitively binds to the receptor. The '806 patent teaches using iodinated PTH analogs in the screening method (see col 22, line 55) and determining whether test compounds compete for PTH binding (see col 23, lines 11-12), clearly anticipating claim 28.

Note

It is noted that the nucleic acid SEQ ID NO: 3 taught by patent 5,494,806 is 94.2% similar to instant SEQ ID NO: 1, which is a polynucleotide encoding instant SEQ ID NO: 2 (an alignment of these sequences is attached to this Office Action as Sequence Alignment #2). Therefore, SEQ ID NO: 3 of the '806 patent does not meet the limitations of instant claims 24 or 27, which require a nucleic acid sequence at least 95% identical to a polynucleotide encoding instant SEQ ID NO: 2.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

zch

Bridget E. Burner

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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	2195	96.1	591	2	US-08-468-249A-20
2	2008	88.0	593	4	US-09-631-603-21
3	2002	87.7	593	2	US-08-468-249A-21
4	2002	87.7	593	4	US-09-826-509-563
5	1710	74.9	585	1	US-08-142-439A-6
6	1710	74.9	585	2	US-08-142-551B-125
7	1710	74.9	585	2	US-08-869-477-6
8	1710	74.9	585	2	US-08-468-249A-19
9	1551	67.9	515	2	US-08-468-249A-18
10	1465	64.2	536	4	US-09-449-632-2
11	1130	49.5	542	4	US-09-449-632-4
12	1068	46.8	575	4	US-09-449-632-5
13	1050.5	46.0	550	4	US-09-631-603-20
14	1044.5	45.8	550	4	US-09-826-509-565
15	1036	45.4	541	3	US-08-468-011A-2
16	1036	45.4	541	3	US-09-236-468A-2
17	1036	45.4	541	5	PCT-US95-07085-2
18	960.5	42.1	207	4	US-08-811-519-31
19	775	34.0	459	4	US-09-694-519-4
20	775.5	34.0	1324	2	US-08-811-897A-56
21	775.5	34.0	1324	3	US-09-201-474-56
22	773.5	33.9	444	4	US-09-694-519-6
23	772	33.8	459	4	US-09-694-519-3
24	772	33.8	459	4	US-09-694-519-8
25	762.5	33.4	458	1	US-08-112-817C-2
26	762.5	33.4	458	4	US-09-694-519-5
27	762.5	33.4	458	4	US-09-694-519-7

SEQUENCE ALIGNMENT

#1

28	757.5	33.2	449	1	US-08-142-439A-5	Sequence 5, Appli
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30	752.5	33.0	457	4	US-09-631-603-23	Sequence 23, Appli
31	752.5	33.0	457	4	US-09-694-519-1	Sequence 1, Appli
32	747	32.7	440	4	US-09-631-603-22	Sequence 22, Appli
33	747.5	32.7	457	4	US-09-826-509-579	Sequence 579, App
34	741	32.5	460	4	US-09-694-519-2	Sequence 2, Appli
35	738	32.3	440	4	US-09-826-509-567	Sequence 567, App
36	718	31.4	447	4	US-09-694-519-9	Sequence 9, Appli
37	687	30.1	448	2	US-08-811-897A-22	Sequence 22, Appli
38	687	30.1	448	2	US-08-855-213-22	Sequence 22, Appli
39	687	30.1	448	3	US-09-201-474-22	Sequence 19, Appli
40	687	30.1	468	4	US-09-631-603-24	Sequence 23, Appli
41	687	30.1	525	2	US-08-811-897A-23	Sequence 23, Appli
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44	684	30.0	448	2	US-08-811-897A-18	Sequence 18, Appli
45	684	30.0	448	2	US-08-855-213-18	Sequence 18, Appli

ALIGNMENTS

RESULT 1
US-08-468-249A-20
; Sequence 20, Application US/08468249A
; Patent No. 5886148
; GENERAL INFORMATION:
; APPLICANT: Segre et al., Gino V.
; TITLE OF INVENTION: PARATHYROID HORMONE RECEPTOR AND DNA
; TITLE OF INVENTION: ENCODING SAME
; NUMBER OF SEQUENCES: 21
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Fish & Richardson P.C.
; STREET: 225 Franklin Street
; CITY: Boston
; STATE: MA
; COUNTRY: USA
; ZIP: 02110-2804
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: Patent in Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/468,249A
; FILING DATE: 06-JUN-1995
; CLASSIFICATION: 530
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US 07/864,475
; FILING DATE: 06-APR-1992
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US 07/681,702
; FILING DATE: 04-MAY-1991
; ATTORNEY/AGENT INFORMATION:
; NAME: Fraser, Janis K.
; REGISTRATION NUMBER: 34,819
; REFERENCE/DOCKET NUMBER: 00786/071003
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 617/542-5070
; TELEFAX: 617/542-8906
; INFORMATION FOR SEQ ID NO: 20:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 591 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
; US-08-468-249A-20

Query Match 96.1%; Score 2195; DB 2; Length 591;
Best Local Similarity 73.6%; Pred. No. 1e-209;
Matches 435; Conservative 0; Mismatches 0; Indels 156; Gaps 1;

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Db	181	REVFDRLGMIYTVGYSVSLASLTAVAILLAYFRRLHCTRNTYHHMPLFUSFMLRAVSIFVK	240
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Db	421	YIVFMATPYTEVSGTLQWQIOMHYEMLFNSFGQFPFVLIYCFNGEVOAEIRKMSWRWTLA	480
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Db	481	LDPKRKARGSSSYSGPMVSHTSVTNVGPRVGLPLSPRLPLTATNGHPQLPGHAKP	540
Qy	384	GAPANET-ETLPTVMAVPKDDGFLNGSCSGLDEASGARPPPLLOSGWETVM	435
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RESULT 3
US-08-468-249A-21
Sequence 21, Application US/08468249A
Patent No. 5886148
GENERAL INFORMATION:
APPLICANT: Segre et al., Gino V.
TITLE OF INVENTION: PARATHYROID HORMONE RECEPTOR AND DNA
TITLE OF INVENTION: ENCODING SAME
NUMBER OF SEQUENCES: 21
CORRESPONDENCE ADDRESS:
ADDRESSEE: Fish & Richardson P.C.
STREET: 225 Franklin Street
CITY: Boston
STATE: MA
COUNTRY: USA
ZIP: 02110-2804
COMPUTER READABLE FORM:
MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: PatentIn Release #1.0, Version #1.30
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/468.249A
FILING DATE: 06-JUN-1995
CLASSIFICATION: 530
PRIOR APPLICATION DATA:
APPLICATION NUMBER: US 07/864,475
FILING DATE: 06-APR-1992
PRIOR APPLICATION DATA:
APPLICATION NUMBER: US 07/681,702
FILING DATE: 04-MAY-1991
ATTORNEY/AGENT INFORMATION:
NAME: Fraser, Janis K.
REGISTRATION NUMBER: 34, 819
REFERENCE/DOCKET NUMBER: 00786/071003

SEQUENCE ALIGNMENT

#2

Db	241	CTGCTGTTTATGCTGCGCGCGGAGCATCTTCGTGAAGAGCGCTGTGCTCTACTCTGCG	300
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Db	361	CCACCTCCGCGCGCGCTGCGCGCGCTAGCTAGCTAGCTAGCTAGCTAGCTAGCTAGCTAGCTAGCT	420
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Qy	454	AGCATCATCTTTCATGCGCGCTTTTCTCAGAGAGAGTACCTGCTGCGGCTTCAACCATCTTT	513
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RESULT 3
117766

LOCUS

DEFINITION

ACCESSION

VERSION

KEYWORDS

SOURCE

ORGANISM

REFERENCE

AUTHORS

TITLE

JOURNAL

FEATURES

source

ORIGIN

Query Match

Best Local Similarity

Matches 1245; Conservative

94.2%; Score 1243.2; DB 6; Length 2051;

99.8%; Pred. No. 3.6e-249; Indels 0; Gaps 0;

Mismatches 3; Indels 0; Gaps 0;

117766

Sequence 3 from patent US 5494806.

117766

117766.1 GI:1598121

Unknown.

Unclassified.

1 (bases 1 to 2051)

Segre, G.V., Kronenberg, H.M., Abou-Samra, A.-B., Juppner, H.,

Potts, J.T., Jr. and Schipani, E.

DNA and vectors encoding the parathyroid hormone receptor,

transformed cells, and recombinant production of PTHR proteins and

peptides

Patent: US 5494806-A 3 27-PEB-1996;

Location/Qualifiers

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ORIGIN

Query Match

Best Local Similarity

Matches 1245; Conservative

94.2%; Score 1243.2; DB 6; Length 2051;

99.8%; Pred. No. 3.6e-249; Indels 0; Gaps 0;

Mismatches 3; Indels 0; Gaps 0;

117766

Sequence 3 from patent US 5494806.

117766

117766.1 GI:1598121

Unknown.

Unclassified.

1 (bases 1 to 2051)

Segre, G.V., Kronenberg, H.M., Abou-Samra, A.-B., Juppner, H.,

Potts, J.T., Jr. and Schipani, E.

DNA and vectors encoding the parathyroid hormone receptor,

transformed cells, and recombinant production of PTHR proteins and

peptides

Patent: US 5494806-A 3 27-PEB-1996;

Location/Qualifiers

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related-peptide receptor"

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373	QY	TGCGCGTGGCGGTGACCTTTCTCTGATCTTCTGGGTACCAACTACTACTGGATCCTTG	432
886	DB	TGCGCGGTGGCGGTGACCTTTCTCTGATCTTCTGGGTACCAACTACTACTGGATCCTTG	945
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673	QY	ATCATCCGGTGTCTGCGCACTAAGCTTCGGGAGACCAATGCGGCGCGCTGTGACACGAG	732
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